

REMARKS

Claims 28, 30, 37, 41, 42 and 44-68 are presently pending. Although Claims 53-68 are withdrawn, they will be eligible for rejoinder upon allowance of the elected claims from which they ultimately depend. Amendments to the claims are discussed below. No new matter has been added herewith. The following addresses the substance of the Office Action.

Obviousness

Claims 28, 30, 37, 40, 42, 48-49 and 51-52 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Klopfenstein et al. (*supra*), in further view of Swerdloff et al. (US 4,517,004), Cookson et al. (2002 *Soil Biology & Biochemistry* **34**:1461-1465), Davis et al. (1956 *J Animal Science* **15**:515-522) and Hamilton (1991 Basic Cattle Nutrition Fact Sheet; <http://www.omafra.gov.on.ca/english/livestock/beef/facts/91-066.htm>)). Claims 28, 49 and 50 were rejected under 35 U.S.C. § 103(a) as being unpatentable over these same references in further view of Schaefer et al. (U.S. Patent No. 5,505,968). Finally, Claims 28, 30, 37, 40-41, 48-49 and 51-52 were rejected under 35 U.S.C. § 103(a) as being unpatentable over the same references with Zerulla et al. (2001 *Biology and Fertility of Soils* **34**:79-84) taking the place of Cookson et al. and Davis et al. However, as described below, the combination of cited references fails to provide any suggestion of “introducing a nitrification inhibitor compound internally to said animal” to result in “reducing loss of nitrogen from the soil,” as presently claimed. In view of the absence of this teaching, the combination of references fails to establish a *prima facie* showing of obviousness.

Summary of Claimed Subject Matter

On Page 11 of the Office Action, the Examiner commented that previous submissions by the Applicant relied on the improved retention of nitrogen within the soil but that the feature was not recited in the claims. However, Claim 28 presently recites that “the nitrification inhibitor affects the conversion of nitrogen containing compounds once the waste is excreted from the animal, thereby reducing loss of nitrogen from the soil as compared to loss of nitrogen from a soil exposed to waste from the animal if said nitrification inhibitor were not introduced.” Thus, the improved retention of nitrogen within the soil is a necessary feature of the presently pending claims, which must be considered in evaluating its patentability.

Applicant also wishes to point out that Claim 28 has been amended to be limited to use of a nitrification inhibitor. Thus, the presently claimed methods no longer read on the use of urease inhibitors that, when administered internally, increase utilization of dietary nitrogen.

Mode of Action of Nitrification and Urease Inhibition

It is important to understand the different cycles for converting nitrogen containing compounds. Importantly, one can not automatically take one type of compound that works in one pathway and substitute it in another pathway. Urease is an enzyme that catalyses the hydrolysis of urea into carbon dioxide and ammonium. In contrast, the nitrification process is bacterial, whereby ammonium is converted to nitrate or nitrous oxide by bacteria. The two processes are unrelated to each other, although one process produces a compound which is the starter of the other. Accordingly, any suggestion relating to urease inhibition would not necessarily be expected by one having ordinary skill in the art to have any bearing on processes relating to nitrate inhibition.

Klopfenstein et al.

In contrast to the presently claimed methods, Klopfenstein is silent regarding introduction of a nitrification inhibitor compound internally to an animal.

Moreover, the disclosure of Klopfenstein et al. is directed to decreasing nutrient excretion through feeding a controlled diet or increasing utilization of the nutrients in the animal. The authors primarily review ways that farmers can control input of nitrogen and phosphorous to minimize output of those nutrients so that they are retained by the animal. As such, Klopfenstein et al. provides no disclosure that would suggest a method resulting in “reducing loss of nitrogen from the soil” as opposed to reducing loss of nitrogen from the animal.

The Examiner referred to page 6 lines 10-14 of Klopfenstein et al. as being one example of a specialized feed additive. However, any reference to feed additives in Klopfenstein et al. is to a substance that will increase the utilization of nutrients within the animal, therefore reducing the likelihood that those substances would be excreted. As stated above, such disclosure provides no suggestion of the presently claimed methods relating to “introducing a nitrification inhibitor compound internally to said animal” resulting in “reducing loss of nitrogen from the soil.”

On Page 11, lines 11 and 12 of the Office Action, the Examiner argued that Klopfenstein et al. teaches the same direction as the present invention. However, as discussed above, the

teachings of Klopfenstein et al. are directed to reducing excretion of compounds, rather than preventing conversion of those compounds after excretion, as presently recited in the claims. Moreover, since the present invention no longer covers urease inhibitors, it is a further step away from the teaching of Klopfenstein et al. Specifically, the invention of the presently pending claims does not require inhibition of conversion of compounds internally, as would be required to reduce excretion of compounds from the animal according to the teachings of Klopfenstein. Thus, the present invention would not achieve the same result as Klopfenstein et al. Indeed, the present invention is not merely an identification of a new advantage of a method taught in the prior art. Rather it is an adaptation which involves using certain compounds to achieve a new result and requiring a unique step, namely "excreting waste from the animal onto the soil, wherein the waste acts as a carrier so that the nitrification inhibitor affects the conversion of nitrogen containing compounds once the waste is excreted from the animal, thereby reducing loss of nitrogen from the soil." Nothing in Klopfenstein et al. or in any of the other cited references would suggest that such a step be carried out.

Swerdloff et al.

The Examiner alleged that Swerdloff et al. suggests administering nitrification inhibitors internally to an animal. The Examiner refers to the disclosure in Swerdloff *et al* of a "nitrification inhibiting dose of the Aryl Phosphoric compounds." However, this disclosure of Swerdloff *et al.* is merely one mention in a long list of possible activities, on the chance that the compounds they discovered did have some of those properties. Specifically, the paragraph bridging columns 8 and 9 provides as follows:

While the composition and method of this invention are particularly suited for agricultural applications for prevention or inhibition of urease catalyzed hydrolysis of urea and/or nitrification, they can also be used in other applications where inhibition of the activity of urease and/or nitrification is desired. For example, such other applications include use as urease inhibitors in animal litters, as feed additives, pharmaceutical applications, urease inhibition in mammalian urinary tracts, and the like. It should be noted that while all of the above referenced compounds exhibit some level of urease inhibiting activity, the particularly active compound employed in one application may not necessarily be useful in another application. Thus, in the selection of a particular active material for use in an application, such factors as toxicity of the material, the environment in which the material will be used, level of urease inhibition desired and the like must be considered in selecting such material.

Thus, the disclosure of Swerdloff et al. suggests that many considerations affect whether a particular compound might be useful for administration internally to an animal, without identifying

even a single compound that might be suitable for such an application. In fact, as discussed in more detail below, Swerdloff et al. identifies only a single compound that has any nitrification-inhibitory activity, and provided no indication that such compound would be suitable for administration internally to an animal.

The Examiner has referenced Tables I, II, and III of Swerdloff et al. as supporting that the disclosed compounds are urease and nitrification inhibitors. Of these tables, only Table III relates to nitrification inhibitors, as Tables I and II of Swerdloff et al. relate to results of urease inhibition tests, which are no longer being claimed. Table III of Swerdloff et al. shows nitrification properties of only one compound, namely Phosphorodiamidic Acid 3 – (1,1'-dimethylethyl)-4-hydroxyphenyl Ester (PDADHE). However, this compound was administered directly to the soil and not “internally to an animal” as presently claimed. Thus, the disclosure of Table III does not support the Examiner’s allegation that Swerdloff et al. suggests the administration of nitrification inhibitors internally to an animal.

Moreover, recent researchers have discounted that any of the Aryl Phosphoric compounds of Swerdloff et al. could have nitrification-inhibiting properties. In this regard, the Applicant submits an Information Disclosure Statement with a copy of Watson, C.J. (2000 in Urease activity and inhibition-principles and practice, presented to the International Fertiliser Society at a meeting in London). This reference specifically indicates at page 26 that one such aryl phosphoric compound, NBPT, has no anti-bacterial activity and therefore is not a nitrification inhibitor. Thus, contrary to the mere allegation of the Swerdloff *et al.* reference, NBPT does not have any affect on conversion of ammonium to nitrate or nitrous oxide. Therefore, while Swerdloff et al. may mention administration of a nitrification inhibiting amount of the Aryl Phosphoric compounds, in practice there can be no reasonable expectation that any of these compounds (a) possess nitrification-inhibiting activity and (b) would be suitable for administration internally to an animal, both of which are required by the presently pending claims. As such, the disclosure of Swerdloff et al. provides no suggestion of “introducing a nitrification inhibitor compound internally to said animal” to result in “reducing loss of nitrogen from the soil,” as presently claimed.

In view of the foregoing, neither of Klopfenstein et al. nor Swerdloff et al. provides any suggestion of this feature of the claimed invention. Additionally, as discussed below, none of the

remaining cited references provide any disclosure that could be combined with these references to create such a suggestion.

Cookson et al.

Cookson *et al* is a study of the effect of dicyandiamide (referred to as DCD in the present disclosure) on conversion of nitrogen in urine. However the reference does not discuss administering the compounds internally into an animal. The study specifically “investigated the effects of DCD on the concentration of NO_3^- -N and NH_4^+ -N in a pastoral soil to which cattle urine has been applied.” Cookson at page 1461, column 1. Thus Cookson discloses only the application of DCD to the soil and not internally to an animal. Nothing in Cookson et al. would suggest anything about “introducing a nitrification inhibitor compound internally to said animal” to result in “reducing loss of nitrogen from the soil,” as presently claimed. As such, Cookson et al. adds nothing to the disclosure of the other references to suggest the presently claimed invention.

Hamilton et al.

Hamilton provides a discussion of animal digestive processes with a focus on animal production. This is inherent from the introduction which reads “The proper nutrition of beef cattle is a key component of a successful production system. Feed usually accounts for the single largest input cost associated with beef cattle.” Hamilton does teach that the rumen is the start of an animal’s digestive track. However, there is nothing in Hamilton that would lead one of ordinary skill in the art to combine that document with any of the other cited document in order to develop a method to reduce emission of nitrogen compounds from land by administering a nitrification-inhibitor compound internally to an animal.

Davis et al.

Davis et al. discloses the internal administration of DCD to animals. However, such internal administration is quite clearly to study the affect of DCD on animal products by studying the levels of urea nitrogen in the blood and milk. There is no consideration in Davis et al. of the compounds being excreted in animal waste. Thus, while Davis et al. may suggest administration of DCD to an animal, it provides not disclosure that would lead one having ordinary skill in the art to conclude that such an administration could lead to “reducing loss of nitrogen from the soil,” as presently claimed.

Schaefer et al.

The Schaefer et al. reference was cited for its disclosure of “the administration of a supplement by adding it to the food or via drench, both of which are oral administration routes.” Office Action at bottom of page 6. As such, the disclosure of Schaefer et al. adds nothing to suggest the invention of the presently claimed invention.

Zerulla et al.

Zerulla et al. was cited for its teaching that DMPP “is non-toxic nitrification inhibitor known to reduce the loss of [sic] minimize the loss of nitrate (nitrogen from soil.” Office Action at bottom of page 8. However, nothing in the reference suggests that DMPP can be administered internally to animals. While the reference does disclose that favorable toxicology and ecotoxicology tests of DMPP were conducted, the reference refers to these as “standard toxicology and ecotoxicology tests.” Zerulla et al. at page 80, second column. Such standard tests do not necessarily imply that DMPP would be suitable for administration internally to animals. Moreover, they certainly do not suggest any reason to so administer the compounds. Accordingly, the disclosure of Zerulla et al. adds no more to the teachings of the remaining references than a disclosure that the DMPP recited in Claim 41 is a known nitrification-inhibiting compound.

Non-obviousness of the Presently Claimed Methods

The Applicant emphasizes that none of the cited references, alone or in combination, suggest administering nitrification-inhibition compounds internally to an animal so as to affect the loss of compounds from animal waste. As such, the cited combination of references fails to suggest the claimed limitation of “excreting waste from the animal onto the soil, wherein the waste acts as a carrier so that the nitrification inhibitor affects the conversion of nitrogen containing compounds once the waste is excreted from the animal, thereby reducing loss of nitrogen from the soil.”

In addition, there is a substantial disconnect between the time of administration and when the compounds have their effect. The Applicant also notes that it is impossible to know whether a compound administered to an animal could be excreted in an active form. There are numerous metabolism pathways *in vitro*, which could alter an administered compound. Further, articles such as Davis et al. disclose the effects of compounds on an animal’s metabolism and absorption

of nutrients. The logical conclusion from Davis et al. is that the administered compounds are processed by the animal and are therefore not expected to be present in the animal waste. Accordingly, there is simply no way for one having ordinary skill in the art to know based on the cited references that internal administration of nitrification-inhibition compounds to an animal would result in any effect in the animal's waste, much less on the soil onto which the waste is excreted. Therefore, even if the references were combined in the manner suggested by the Examiner, there would be no reasonable expectation of success in carrying out the claimed invention.

In view of the foregoing, it is clear that the combination of all of the references fails to provide a disclosure that would lead one having ordinary skill in the art toward "introducing a nitrification inhibitor compound internally to said animal" would result in "reducing loss of nitrogen from the soil," as presently claimed. Without this suggestion, there can be no *prima facie* showing of obviousness. Moreover, even if there were such a suggestion (which there is not) nothing within the knowledge of those having ordinary skill in the art would provide any indication that a reasonable expectation of success would be obtained if an attempt were made to achieve these results. Such a reasonable expectation of success would also be required to establish a *prima facie* showing of obviousness. Furthermore, any suggestion in the prior art relating to urease inhibition would not be directly applicable to the presently claimed invention. Accordingly, no proper *prima facie* showing of obviousness can be established on the basis of the presently cited references.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of Applicants' amendments to the Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: February 22, 2011

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